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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/343,406	ENDL ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46,48 and 51-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46, 48, and 51-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 46, 48, and 51-54 are pending.

2. The disclosure is objected to for failing to comply with the requirements of 37 C.F.R. 1.821 through 1.825, specifically, SEQ ID NO is required for page 4, 5, and brief description of the drawing for Figures 1 and 2 on page 25. Appropriate correction is required.

3. In view of the amendment filed 7/10/3, the following rejections remain.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 46, 48, and 51-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for making and/or using a peptide with the sequence of one of SEQ ID NO: 2, 3 or 20-39 for detection of autoantigen reactive T cells, **does not** reasonably provide enablement for making and/or using any isolated peptide/derivative and pharmaceutical composition, thereof wherein the peptide derived from glutamic acid decarboxylase having a length of 10 to 25 amino acids that is at least 50% homologous to the peptide of at least 10 continuous amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO: 2, 3 and 20-39 and includes anchor positions for binding to alleles of human MHC class II molecules DR3 or DR4, wherein the peptide derivative is not SEQ ID NO: 19 and wherein the alleles of MHC class II are selected from the group consisting of DR B1 301, DR B1 401, DR B1 402, and DR B1 404 wherein in said peptide derivatives the peptide backbone and or the reactive amino acid side groups are derivatized as set forth in claims 46, 48, 51-54 for treating any disease.

The specification discloses only SEQ ID NO: 2, 3 and 20-39 (especially sequence listing and Figures 1 and 2), but no peptides or peptide derivatives of at least 10 amino acids and up to 25 amino acids from one of SEQ ID NO: 2, 3 and 20-39, other than SEQ ID N0: 4-18 which are 12-mer, l4-mer, 18-mer and 20-mer peptide subsequences derived from SEQ ID NO: 2 (especially page 38 and sequence listing).

The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claims encompass peptides of between 10 and 25 amino acid residues in length which contain at least 10 amino acid residues, potentially from any one SEQ ID NO: 2, 3 or 20-39, and peptides of between 10 and 25 amino acid residues in length wherein "at least 50% of the peptide backbone and the reactive amino acid group are derivatized". There is insufficient guidance as to which amino acids within any one SEQ ID NO: 2, 3 or 20-39 can be substituted for which undisclosed amino acids. Further, the term "comprising" is open-ended. It expands the undisclosed peptides to include additional amino acids at either or both ends, let alone which undisclosed peptide would still maintain binding specificity and affinity T cell receptor having a particular MHC class II molecule as SEQ ID NO: 2, 3 or 20-39. Peptides with the same specificity/and or affinity encompass peptides of sequence unrelated to the claimed peptides. The state of the art is such that it is unpredictable in the absence of appropriate evidence whether the claimed invention can be made and or used. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Further, there is no in vivo working example in the specification as filed that the claimed pharmaceutical composition comprising the undisclosed peptide or peptide derivative could treat any disease.

The specification does not disclose the definition of "a specificity or/and affinity" which is equivalent to that of the aforementioned peptides which contain at least 10 amino acid residues from SEQ ID NO: 2, 3 or 20-39, and which contains anchor residues for binding to the said class 11 MHC molecules. The specification discloses the term essentially equivalent specificity or/and affinity of binding to MHC molecules" includes an improved binding specificity or/and affinity compared to the amino acid sequences SEQ ID NO: 2, 3 or 20-39 (especially page 8 at the second 111 paragraph). The specification further discloses that the term peptide derivatives includes peptides in which one or several amino acid residues have been derivatized by a chemical reaction (especially page 8 at the last paragraph). The specification discloses that an object of the invention is to provide new auto-reactive peptides which react with T cells from type I diabetics, and that this object is achieved by peptides or derivatives which bind analogously which are suitable for the detection, isolation, proliferation, anergization or/and elimination of auto-reactive T cells (especially paragraph spanning pages 3 and 4). The specification discloses, on page 7 of the instant specification, at the last paragraph that anchor position" means an amino acid residue

essential for binding to an MHC molecule and in particular to an MHC molecule of classes DR3, DR4 or DQ. The specification further discloses at lines 8-10 of the last paragraph that the anchor positions for the DRB10401 binding motive (motif are given in Hammer et al, Cell 74, 1993, pp 197-200. Evidentiary reference Rammensee et al (Immunogenetics, 1995, of record) teaches that peptides of more than 9 amino acid residues in length bind to MHC class II molecules.

The length of the peptide is important for binding to HLA (along with the presence of anchor (or "motif') amino acid residues present within the peptide). In addition, the minimum amount of peptide required to span the binding groove and make favorable contacts may be dependent upon the sequence of the peptide itself since different amino acid residues have different physicochemical properties, and may be dependent upon the identity of the additional amino acids, since these residues may make a negative contribution to binding. Rammensee et al further teach that epitope prediction is not as easy for class II ligands as for class I ligands because the anchors are more degenerate in their specificity. Rammensee et al teach the need for algorithms based upon side chain contribution of each amino acid residue at each position in the peptide ligand, and the teaching of Hammer et al referred to by Rammensee et al and also by the Applicant's amendment to the specification –to incorporate a table from Hammer et al at page 2 of Applicant's amendment filed 1/4/02) is for one allele of HLA-DR4, Drp 1*0401.

Evidentiary reference Smilek et al (IDS) teach that a single amino acid change in an autoreactive peptide from myelin basic protein confers the capacity to prevent rather than induce the autoimmune disease EAE. Accordingly, there is a high level of unpredictability in designing/selecting sequences that would still maintain function, let alone a peptide derivative with 50% homology. There is insufficient as to which amino acid residue within any of the peptide of SEQ ID NO: 2, 3 and 20-39 can be substituted, and deleted and whether the resulting peptide would still bind, and maintain function, in turn, would be useful for treating any disease. Given the indefinite number of disease, a pharmaceutical composition in the absence of in vivo working example is unpredictable for the following reasons: (1) the peptide may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the peptide; (2) the peptide may not reach the target area because, i.e. the peptide may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the peptide unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex

parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992). Because of this lack of guidance, extended experimentation that would be required to determine which substitutions/deletions/additions or permutations of amino acids would be necessary to provide the desired activity. Since it would require undue experimentation to identify amino acid sequences that have functional activity, it would require undue experimentation to make and use the corresponding peptides. Therefore, undue experimentation would be required to determine what peptides could or could not be used in the claimed invention. There is insufficient guidance in the specification as to how to make and/or use the instant invention. Undue experimentation would be required of one skilled in the art to practice the instant invention. The enablement provided by the specification is not commensurate with the scope of the claims. See In re Wands 8 USPQM 1400 (CAFC 1988).

Applicant's arguments in the amendment filed 7/10/03 have been fully considered but they are not persuasive.

Applicants' position is that the claims have been amended to recite peptides having at least 10 contiguous amino acids of the disclosed sequences or sequences that are least 50% homologous to these sequences, have an affinity or specificity that is essentially equivalent to the disclosed peptide sequences and wherein the peptides include anchor positions for binding addition, the specification teaches that human MHC DR3 or DR4 alleles, the proliferation assay adequate assay for with GAD-specific determining reactivity of a cell lines provides an peptide with DR3 or DR4 alleles. Furthermore, the number of possible peptides consisting of 10 consecutive amino acids of SEQ ID NO: 2, 3 and 20-39 and these can readily be determined without undue experimentation.

However, the terms "having" and "comprising" are open-ended. It expands the peptide, peptide derivative to include additional amino acids at either or both ends. There is insufficient guidance as to which amino acids to be added and whether it would bind and retain function such that it is useful as a pharmaceutical composition for treating any disease. Even if the peptide or peptide derivative is limited to a length of between 10 to 25 amino acids, a 50% homology means 50% difference, which translate to having 5 to 12 amino acids differences. Rammensee et al, of record, teach that epitope prediction is not as easy for class II ligands as for class I ligands because the anchors are more degenerate in their specificity. Smilek et al (IDS) teach that a single amino acid change in an autoreactive peptide from myelin basic protein confers the capacity to prevent rather than induce the autoimmune disease EAE. Further, there is insufficient

guidance as to the function of any peptide and peptide derivative having only 50% homology to SEQ ID NO: 2, 3, and 20-39. Further, there is no in vivo working example demonstrating any peptide or peptide derivative for treating any disease. Given the indefinite number of disease, a pharmaceutical composition in the absence of in vivo working example is unpredictable for the following reasons: (1) the peptide may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the peptide; (2) the peptide may not reach the target area because, i.e. the peptide may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the peptide unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992). For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

6. Claims 46, 48, and 51-54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter" , Vas-cath, Inc. V. Mahurkar, 19 USPQZd 11 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of the claimed: any isolated peptide/derivative and pharmaceutical composition, thereof wherein the peptide derived from glutamic acid decarboxylase having a length of 10 to 25 amino acids that is at least 50% homologous to the peptide of at least 10 continuous amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO: 2, 3 and 20-39 and includes anchor positions for binding to alleles of human MHC class II molecules DR3 or DR4, wherein the peptide derivative is not SEQ ID NO: 19 and wherein the alleles of MHC class II are selected from the group consisting of DR B1 301, DR B1 401, DR B1 402, and DR B1 404 wherein in said peptide derivatives the peptide backbone and or the reactive

amino acid side groups are derivatized as set forth in claims 46, 48, 51-54 for treating any disease.

The instant claims encompass a peptide/derivative/pharmaceutical composition, thereof of at least 6 amino acid residues of an amino acid sequence of one of SEQ ID N0: 2, 3 or 20-39, or consisting of between 6 and 25 amino acids which comprises at least 6 amino acid residues of one of SEQ ID NO: 2, 3 or 20-39. The said peptide/derivative/pharmaceutical composition, thereof can comprise amino acid residues that flank the said sequences in the peptide or protein of origin, or can be any number of undisclosed and unrelated sequences, and the at least 6 amino acid residues may not be contiguous with each other in the peptide/derivative. There is insufficient disclosure in the specification on peptides of between 6 and 25 amino acids comprising at least 6 amino acid residues selected from the group consisting of SEQ ID NO: 2, 3 and 20-39.

The specification discloses only SEQ ID NO: 2, 3 and 20-39 (especially sequence listing and Figures 1 and 2), but no peptides or peptide derivatives of at least 10 amino acids and up to 25 amino acids from one of SEQ ID NO: 2, 3 and 20-39, other than SEQ ID N0: 4-18 which are 12-mer, l4-mer, 18-mer and 20-mer peptide subsequences derived from SEQ ID NO: 2 (especially page 38 and sequence listing). The specification discloses, on page 7 of the instant specification, at the last paragraph that "anchor position" means an amino acid residue essential for binding to an MHC molecule and in particular to an MHC molecule of classes DR3, DR4 or DQ. The specification further discloses at lines 8-10 of the last paragraph that the anchor positions for the DRR10401 binding motive (motif are given in Hammer et a1., Cell 74, 1993, pp 197-200.

The specification does not disclose any 10-25 mer peptide sequences that is "50% homologous to any peptide of SEQ ID NO: 2, 3 and 20-39", let alone binding to MHC class II allele such as DR B1, 301, DR B 401, DR B1 402, and DR B1 404. Other than the specific peptides mentioned above, there is inadequate written description about the structure associated with function such as 10-25 mer peptide sequences that is "50% homologous to any peptide of SEQ ID NO: 2, 3 and 20-39". There is inadequate written description about which amino acid residues within SEQ ID NO: 2, 3 and 20-39 can be substituted for which undisclosed amino acids and/or deleted and whether the resulting peptide has function other than simply binding, in turn, would be useful for a pharmaceutical composition for treating a specific disease, including autoimmune diabetes.

In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. A generic statement such as "a peptide or peptide derivative having a length of 10 to 25 amino acids that is at least 50% homologous to the peptide selected from the group consisting of SEQ ID NO: 2, 3 and 20-39" does not define the structure of the peptide without the specific amino acid sequence.

"A peptide or peptide derivative having a length of 10 to 25 amino acids which exhibits a specificity or/and affinity which is essentially equivalent to that of the peptide (a) and includes anchor positions for binding to alleles of MHC class II molecules DR3 or DR4" recited in the instant claims does not describe the claimed peptide/derivative, except by the property of containing at least 10-25 amino acid residues from one of SEQ ID NO: 2, 3 or 20-39 or being a peptide or derivative thereof that exhibits some type or degree of specificity or/and some type or degree of affinity and includes anchor residues for binding to the recited alleles of HLA-DR3 or HLA-DR4. It does not specifically define any of the peptides/derivatives that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others, other than in the former case, that they comprise at least 10 amino acid residues found in one of SEQ ID NO: 2, 3 or 20-39, and in the latter case that they contain anchor residues for binding to an allele of HLA-DR3 or HLA-DR4 recited in the instant claims. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. In addition, a definition by function does not suffice to define the genus because it is only an indication of what the property the peptide has, rather than what it is. See Fiers, 984 F.2d at 1169-71, 25 USPQZd at 1605-06. It is only a definition of a useful result rather than a definition of what achieves that result. Many such species may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outline (el goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate. ").

Not only the structure of the peptide and derivative thereof is not disclosed, it is not clear the undisclosed peptide and derivative thereof has any function since the undisclosed peptide or peptide derivative is at least 50% different from SEQ ID NO: 2, 3 and 20-39, in turn, would be useful for a pharmaceutical composition for treating any disease. Given the indefinite number of

disease, the pharmaceutical composition comprising the undisclosed peptide or derivative thereof is not adequately described. Given the lack of additional example of peptide or derivative for a pharmaceutical composition for treating any disease, one of ordinary skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed.

Applicant's arguments in the amendment filed 7/10/03 have been fully considered but they are not persuasive.

Applicants' position is that the claims have been amended to recite peptides having at least 10 contiguous amino acids of the disclosed sequences or sequences that are least 50% homologous to these sequences, and anchor positions common functional for binding specific MHC class II alleles and reactivity with the specific recited human MHC class alleles.

However, the specification discloses only SEQ ID NO: 2, 3 and 20-39 (especially sequence listing and Figures 1 and 2), but no peptides or peptide derivatives of at least 10 amino acids and up to 25 amino acids from one of SEQ ID NO: 2, 3 and 20-39, other than SEQ ID N0: 4-18 which are 12-mer, l4-mer, 18-mer and 20-mer peptide subsequences derived from SEQ ID NO: 2 (especially page 38 and sequence listing).

The specification does not disclose any 10-25 mer peptide sequences that is "50% homologous to any peptide of SEQ ID NO: 2, 3 and 20-39", let alone binding to MHC class II allele such as DR B1, 301, DR B 401, DR B1 402, and DR B1 404 for a pharmaceutical composition for treating any disease. Other than the specific peptides mentioned above, there is inadequate written description about the structure associated with function such as 10-25 mer peptide sequences that is "50% homologous to any peptide of SEQ ID NO: 2, 3 and 20-39". There is inadequate written description about which amino acid residues within SEQ ID NO: 2, 3 and 20-39 can be substituted for which undisclosed amino acids and/or deleted and whether the resulting peptide has function other than simply binding, in turn, would be useful for any purpose. Since the peptide and derivative thereof is not adequately described, it logically follows that the pharmaceutical composition comprising said undisclosed peptide and derivative thereof is not adequately described.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 46, 48, and 51-53 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 95/07992 (of record) as evidenced by Rnmmensee et al (Immunogenetics, Vol. 41, 178-228, 1995, of record).

WO 95/07992 teaches various 20-mer polypeptides such as **NMYAMMIARFKMFP**EVKEKG and **LLYGDAEKPAESSGG**SQPPRA (reference SEQ ID NO: 17, Table 11 on page 76, in particular). The reference peptides are at least 50% homologous to the claimed peptide NMYAMMIARFKMFP (SEQ ID NO: 30) and LLYGDAEKPAESGG (SEQ ID NO: 24). WO 95/07992 also teaches a peptide such as DE**RGKMIPSDLERRIL**EAKQ which is at least 50% homologous to the claimed peptide of Glu Arg Gly Lys Met Ile Pro Ser Asp Leu Glu Arg Arg Ile Leu Glu Ala Lys Gln Lys (SEQ ID NO: 3). WO 95/07992 teaches the peptide linked to a label, i.e., a marker, that is a radioisotope, a lectin, a drug, or a toxin. WO 95/07992 teaches that lectins can stimulate T cells, i.e., are an accessory stimulating component. WO 95/07992 teaches pharmaceutical administration of the said peptide in pharmaceutically acceptable carriers). WO 95/07992 teaches that peptides from gad having at least one determinant for binding to T-cell MHC receptor can be produced or chemically synthesized (especially claims 1, 15, 18, 26 and pages 17, 18 and 27). Given that the reference peptides have a long stretch of 14 identical amino acids as the claimed peptides, the reference peptides inherently have affinity and binding specificity as the claimed peptides. The claimed peptide appears to be the same as the art absent a showing of any differences. Since the Patent Office does not have the facilities for examining and comparing the molecule of the instant invention to those of the prior art, the burden is on applicant to show an unobvious distinction between the molecule of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). Thus, the reference teachings anticipate the claimed invention.

Applicant's arguments filed 7/10/03 have been fully considered but they are not persuasive.

The claims have been amended and do not recite peptides that bind to the DRB1*101 MHC allele.

However, the reference peptides such as **NMYAMMIARFKMFP**EVKEKG and **LLYGDAEKPAESSGG**SQPPRA (reference SEQ ID NO: 17, Table 11 on page 76, in particular) and are at least 50% homologous to the claimed peptide NMYAMMIARFKMFP (SEQ ID NO: 30) and LLYGDAEKPAESGG (SEQ ID NO: 24). Given that the reference peptides have a long stretch of 14 identical amino acids as the claimed peptides, the reference peptides inherently have affinity and binding specificity as the claimed peptides. The claimed peptide appears to be the same as the art absent a showing of any differences. Since the Patent Office does not have the facilities for examining and comparing the molecule of the instant invention to those of the prior art, the burden is on applicant to show an unobvious distinction between the molecule of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). Thus, the reference teachings anticipate the claimed invention.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claim 54 is rejected under 35 U.S.C. 5 103(a) as being unpatentable over WO 95/07992 (of record) in view of U.S. Patent No. 5,750, 114 (of record) and Smilek et al (of record, Proc. Natl. Acad. Sci. USA, 88, 9633-9637, 1991, IDS).

WO 95/07992 teaches various 20-mer polypeptides such as **NMYAMMIARFKMFP**EVKEKG and **LLYGDAEKPAESSGG**SQPPRA (reference SEQ ID

NO: 17, Table 11 on page 76, in particular). The reference peptides are at least 50% homologous to the claimed peptide NMYAMMIARFKMFP (SEQ ID NO: 30) and LLYGDAEKPAESGG (SEQ ID NO: 24). WO 95/07992 also teaches a peptide such as **DERGKMIPSDLERRIL**EAKQ which is at least 50% homologous to the claimed peptide of Glu Arg Gly Lys Met Ile Pro Ser Asp Leu Glu Arg Arg Ile Leu Glu Ala Lys Gln Lys (SEQ ID NO: 3). WO 95/07992 teaches the peptide linked to a label, i.e., a marker, that is a radioisotope, a lectin, a drug, or a toxin. WO 95/07992 teaches that lectins can stimulate T cells, i.e., are an accessory stimulating component. WO 95/07992 teaches pharmaceutical administration of the said peptide in pharmaceutically acceptable carriers). WO 95/07992 teaches that peptides from gad having at least one determinant for binding to T-cell MHC receptor can be produced or chemically synthesized (especially claims 1, 15, 18, 26 and pages 17, 18 and 27). Given that the reference peptides have a long stretch of 14 identical amino acids as the claimed peptides, the reference peptides inherently have affinity and binding specificity as the claimed peptides. The claimed peptide appears to be the same as the art absent a showing of any differences. Since the Patent Office does not have the facilities for examining and comparing the molecule of the instant invention to those of the prior art, the burden is on applicant to show an unobvious distinction between the molecule of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

WO 95/07992 does not teach a pharmaceutical composition comprising an accessory stimulating component that is a cytokine.

U.S. Patent No. 5,750, 114 discloses pharmaceutical compositions comprising peptides and further comprising immunomodulators such as IL-2, i.e. , a cytokine, for human administration (especially column at lines). U.S. Patent No. 5,750,114 further discloses that the choice of an adjuvant for the species of the individual being vaccinated when that species is human, depends partially upon whether or not the adjuvant has been approved for human use by the FDA (especially column 4 at lines 23-45).

Smilek et al teach administration of autoreactive mbp peptides along with an adjuvant, complete Freunds adjuvant (CFA), i.e., an immunomodulator (especially Example 4), to mice.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have added an adjuvant as taught by Smilek et al or cytokine such as lL-2 disclosed by U.S. Patent No. 5,750, 114 to the gad peptide-containing pharmaceutical composition taught by WO 95/07992.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to immunomodulate an immune response to gad peptides in humans because U.S. Patent No. 5,750,1 14 discloses use of peptides comprising immunomodulating cytokines, Smilek et al disclose administration of autoreactive mbp peptides along with an adjuvant CFA in mice, WO 95/07992 teaches pharmaceutical compositions comprising autoreactive gad peptides for human usage and U.S. Patent No. 5,750, 114 discloses pharmaceutical compositions comprising peptides and an immunomodulator such as IL-2, i.e., a cytokine, for human administration. In addition, one of ordinary skill in the art at the time the invention was made would have been aware that CFA adjuvant taught by Smilek et al was contraindicated for human usage due to the heat killed mycobacterial component in CFA.

Applicant's arguments filed 7/10/03 have been fully considered but they are not persuasive.

The claims as amended do not recite the gad-peptide containing pharmaceutical composition as taught by WO95/07992.

However, the amended claims still read on the reference peptides. WO 95/07992 teaches various 20-mer polypeptides such as **NMYAMMIARFKMFP**EVKEKG and **LLYGDAEKPAESSGG**SQPPRA (reference SEQ ID NO: 17, Table 11 on page 76, in particular). The reference peptides are at least 50% homologous to the claimed peptide NMYAMMIARFKMFP (SEQ ID NO: 30) and LLYGDAEKPAESGG (SEQ ID NO: 24). WO 95/07992 also teaches a peptide such as D**ERGKMIPSDLERRIL**EAKQ which is at least 50% homologous to the claimed peptide of Glu Arg Gly Lys Met Ile Pro Ser Asp Leu Glu Arg Arg Ile Leu Glu Ala Lys Gln Lys (SEQ ID NO: 3). WO 95/07992 teaches the peptide linked to a label, i.e., a marker, that is a radioisotope, a lectin, a drug, or a toxin. WO 95/07992 teaches that lectins can stimulate T cells, i.e., are an accessory stimulating component. WO 95/07992 teaches pharmaceutical administration of the said peptide in pharmaceutically acceptable carriers). WO 95/07992 teaches that peptides from gad having at least one determinant for binding to T-cell MHC receptor can be produced or chemically synthesized (especially claims 1, 15, 18, 26 and pages 17, 18 and 27). Given that the reference peptides have a long stretch of 14 identical amino acids as the claimed peptides, the reference peptides inherently have affinity and binding specificity as the claimed peptides. The claimed peptide appears to be the same as the art absent a showing of any differences. Since the Patent Office does not have the facilities for examining and comparing the molecule of the instant invention to those of the prior art, the burden is on

applicant to show an unobvious distinction between the molecule of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

12. The following new grounds of rejection are necessitated by the amendment filed 7/10/03.

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 46, 48, and 51-54 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

The "a peptide ...at least 50% homologous to the peptide of (a) ...wherein the peptide derivative is not SEQ ID NO: 19" in Claims 46 and 48 represents a departure from the specification and the claims as originally filed. Applicant has not pointed out the support for said phrase.

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

16. Claim 46, 48, and 51-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "said peptide derivatives" in claims 46, line 15, and claim 48, line 14 lacks antecedent basis in base claim 46 and 48 because the word "derivatives" is not mentioned before.

The "accessory stimulating component" in claim 53 is indefinite and ambiguous because it is not clear which "component" is accessory stimulating component. One of ordinary skill in the art cannot appraise the metes and bound of the claimed invention.

17. No claim is allowed.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (703) 872-9306.

20. Any Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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February 9, 2004

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